Voxel-Wise Estimation of Hemodynamic Onset Delays During a Lexical Decision Task

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Introduction and Objectives

Differences in reaction time latencies during lexical decision tasks may occur due to phonological, graphemic, orthographic, or semantic processing. The use of Functional Magnetic Resonance Imaging (FMRI) to dissociate these possibilities has been limited due to the complexity of their relationship and limitations set by the FMRI experimental environment. High temporal resolution FMRI may allow for spatially precise estimates of the locus of the RT delay and thus the neural network responsible for the delay to be determined.

The temporal resolution of FMRI is believed to be limited due to the relatively slow temporal characteristics of the hemodynamic response. Recently, several investigators have demonstrated that delays in the hemodynamic response correlate well with reaction time differences in simple motor tasks and mental rotation experiments[1,2]. Region of interest estimation of the temporal characteristics of the hemodynamic delay was the method used in both these studies. We believe that while the temporal properties of the hemodynamic response vary greatly between voxels that they remain stable within voxels. This would allow for a spatially selective estimation of precise temporal processing within active neural circuits to be estimated using FMRI.

The present study was conducted to investigate whether the temporal characteristics of the hemodynamic response are stable enough, within a voxel, to allow for estimation of neural network timing within a complex cognitive task, using the spatial resolution afforded by FMRI.

1. Menon R, et al. (1998). PNAS, U.S.A. Vol. 95, 10902-10907.

Richter W., et al. (2000). Journal of Cog. Neuro., Vol 12:2, 310-320

Methods

Subjects:

Six subjects (2 women) participated.

Independent Variables:

*Tasks differed with respect to **LEXICAL PROPERTIES***
(Words vs. Pronounceable Non-Words)
OR
*By the **STIMULUS ORIENTATION***
(Rotated 0º vs. 120º)

Behavioral Tasks:

1)Lexical Decision:
Subjects were presented with six letter words or pronounceable Non-Words and instructed to respond with an appropriate key press. Random presentations of the Words and Non-Words were presented with no rotation, 60 degree, or a 120-degree rotation.

2) Fixation: *(Baseline)*
Subjects were simply instructed to fixate on a cross hair.

3)Rotation Control*: (Data not presented)*
Subjects responded to the orientation of a set of nonsense characters

Data Analyses

Individual Time Series:

1. All four scanning series were concatenated and motion corrected.

2. Deconvolution was performed using the AFNI statistical software package for each trial type. From this analysis an Impulse Response Function (IRF; hemodynamic transfer function) for each whole brain voxel is derived. Additional statistics vs. baseline and general linear post-hoc comparisons were also calculated.

3. Hemodynamic Delay estimates were calculated on a voxel-wise basis using the Hilbert-Delay transform applied to the cross-correlation function using a Gamma Variate transfer function and the IRF. The delay maps were then thresholded using the contingent cross-correlation coefficient.

4. Subjects data were transformed in standard stereotaxic space.

5. Signed F-statistics from Post-Hoc GLT's, between word and non-word conditions, and rotated and non-rotated conditions were transformed into t-statistics.

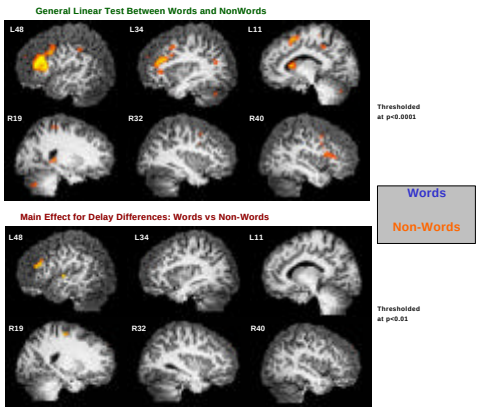
Group Analyses:

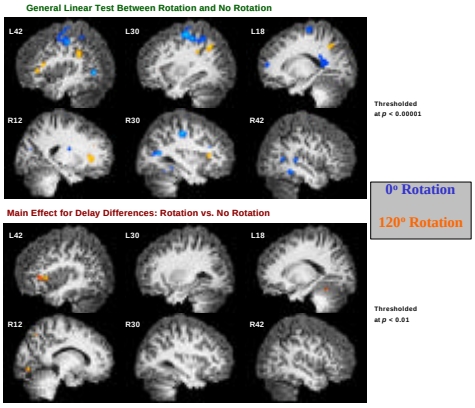
1) A whole-brain voxel-wise ANOVA was conducted among the post-hoc t-statistics for the LEXICAL and ORIENTATION comparisons.

2) Delay maps were submitted to a two-way ANOVA with LEXICAL and ORIENTATION as the factors of interest.

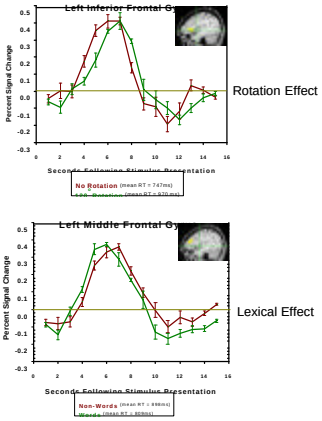
Individual Region of Interest Analyses:

1) Group Regions of Interest maps were created from the Group Delay Analyses, resampled to individual subjects data. Only active voxels within these masks are presented below.

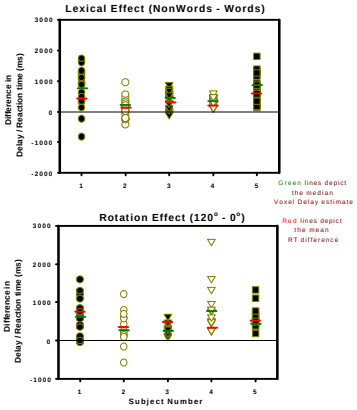




Mean Impulse Response Functions for Activated Voxels



Delay Differences from Indivdual Voxels within the Above ROI's



Results and Conclusions

1) **Lexical decision performance was not affected by stimulus rotation as subjects performed 94% and 91% correct on the non-rotated and rotated stimuli, respectively.**

2) **Statistical comparisons of the magnitude of response to words and non-words showed much less spatial selectivity than maps created using delay estimates. Many regions showed differences in signal magnitude between words and non-words but only the Middle Frontal gyrus, Superior Temporal gyrus and supplementary motor areas showed significant differences in hemodynamic onset delays.**

3) **Although delay estimates of individual voxels within active regions showed a high degree of variability, these estimates were generally within the same degree of magnitude as expressed through RT measures. In the future, this variability may further be reduced as better methods of estimating/modeling the hemodynamic response are improved.**

4) **This study demonstrate that voxel-wise estimation of hemodynamic response onsets has utility within the realm of understanding the neural systems involved in higher order cognitive processing.**